UNIVERSITY OF LONDON

POSTGRADUATE MEDICAL SCHOOL
OF LONDON

Telegrams
POSGRADMED CHISK LONDON
Telephone
SHEpherds Bush 1260 (4 lines)

DUCANE ROAD
LONDON, W.12

P.S. Many thanks for the Christmas card, & kindest regards to Pupa (is Albamaria her proper name?) from Nora & me. I hope you did not have too tiring a Christmas.

N.B. Final results of F+ analysis of prototrophs from three separate 58/F- × W/F+ crosses — 5/14 F+, 8/25 F+ & 11/30 F+.
Would you like to exchange 58/F- strains?

20th December, 1952.

My dear Luca,

Many thanks for your letter. A few points of business first before I forget them. Reprints: The C.U.S. wrote me that the maximum number they can send the Author is 200 + 25 free. Institutes, however, are allowed 500. I have therefore done the best I can for you and arranged for you to have 225 and the Institute to get 300. The C.U.S. have agreed to this so you will in effect have not far short of the 600 you wanted. Standfast rung up the other day and said he was not sure whether, after all, your new ending could go in since the rather extensive deletions mean that a whole page would probably be left blank. I have therefore sent him your alternative ending and he will do the best he can about it. I have sent on the 2 references and the "strain No.8" alteration. I do not think the "#8" would be generally understood, though perhaps the general reader is not so ignorant as I! WORK! I have spent (wasted) quite a lot of time looking round for an opening in the K-12 story. Only within the last few weeks have I hit upon what seem to me to be two promising lines. The first seems closely related, once again, to what you are doing. Jim Watson suggested, as the result of the azide segregations, & probably with your F^r story at the back of his mind, that it might be worth seeing if there was any evidence of F+ segregation in the reversed 58 X W677 cross. I had only tested 58/F+ X W/F- prototrophs for F+ previously. I find that whereas 100% 58/F+ X W/F- prototrophs are still F+, only 30% 58/F- X W/F+ prototrophs are F+! I have done 2 series on different crosses (14 & 25 prototrophs) with the same result and have a 3rd. series of 30 which will be read tomorrow. Like you, I reasoned that this is either due to segregation of to instability of F+ in 58/F-, and favoured the latter since F+ is transduced to 58/F- much less efficiently than to W/F- while a change in the cell favouring instability would help to explain why 58 had become F- in the first place. I thought I could differentiate these two possibilities by means of F+ X F+ crosses, by testing for F+ those prototrophs which were Lac+Mal+ and which (according to me, anyway) had been formed from W/F+ and 58 behaving as a gene acceptor (i.e. F-, either due to instability ~~of~~ or phenocopy). I found, however, that all Lac+Mal+ prototrophs from both 58/F+ & (58/F- transduced to F+) were F+ when crossed with W/F+. I had hoped to find them 100%F+ when 58/F+ was used and only 30%F+ when (F- transduced to F+) was used. This would have eliminated segregation and linkage of F+. I hope this is clear — it is'nt very well expressed. I suppose these results could be explicable if F+ had more than one possible locus, one being very close to Leucine (F+ being retained here in 58/F+ behaving as an F- phenocopy) and the other being just distal to B_1 on

(or, if Jim W. is right, one F+ for each chromosome! There are many here).

the B_1-M bit of chromosome. I will test this but it doesn't seem very promising to me, especially since your work on F^r which I take to be another facet of the same problem. My second finding is this. I normally make my crosses by mixing young broth cultures (either static or aerated) and washing at once. I have done several hundred separate (but limited) analyses and the results are strikingly consistent. In analysis of 100 prototrophs from 3 separate crosses (58/F+ X W/F-) I get 30, 34 & 42% Lac+Mal- crossovers and 12, 11 & 16% Az^s prototrophs when the F- parent is Az^s. Analysis of 100 prototrophs from the same cross in which an aliquot of the 58/F+ culture from the 3rd. cross was suspended in buffered saline for 1½ hrs. before mixing with W/F- gave a different result — only 14% Lac+Mal- c.o.s and 32% Az^s. This seems significant to me and I would explain it by supposing that the saline treatment tends to eliminate the larger chromosome segments issuing from the F+ parent and leave only those carrying TL. This will obviously require a lot of work and I also want to try the effect of shaking & of DNA-ase (using SM to "freeze" the F+ culture after washing free of DNA-ase) on the genetic pattern of prototrophs. I think it possible that if F+ is a gene vector (I haven't abandoned this idea yet), different physical conditions may strip DNA from it in different ways and that an explanation of the F- phenocopy may lie along these lines. I will be interested in what you think.

You will be interested to hear that I learn I will be asked to contribute to the next Cold Spring Harbor Symposium on viruses! It seems a bit thin to me & I will clearly have to work hard at this end of the business. I am sorry you won't be there, but I suppose that if this aspect of the K-12 story was considered worth including, my SM & UV work gave me preferential entitlement. Best of luck — Bill